

1. (Amended) A method for producing a cloned ungulate wherein the expression of both copies of a gene essential for B cell production has been knocked out, wherein said gene is IgM, which comprises the following steps:

(i) producing a male and/or female ungulate cell wherein the expression of one or both copies of the IgM heavy chain has been eliminated by targeted disruption;

(ii) using said cell or DNA therefrom as a donor for nuclear transfer by fusing or inserting said donor cell or nucleus into an oocyte or blastomere, which is enucleated before or after transfer, activating the resulting nuclear transfer unit and/or the oocyte prior or simultaneous to nuclear transfer and culturing in a suitable medium to produce a nuclear transfer embryo;

(iii) introducing said nuclear transfer embryo into a female ungulate; and

(iv) obtaining a cloned fetus or animal ungulate that expresses the genotype of the donor differentiated cell, in which one or both copies of the IgM (mu) chain gene have been eliminated: and

(v) optionally, mating said cloned male or female ungulate with another cloned female ungulate wherein one copy of the IgM gene has been knocked out and selecting progeny wherein both copies of the IgM genes have been knocked out.

2. (Amended) The method of Claim 1, wherein the expression of both copies of the IgM heavy chain (mu) gene is eliminated, by a three-step process comprising the following steps:

(i) a desired ungulate cell is contacted with a DNA construct that provides for targeted deletion or inactivation of said IgM (mu) gene by homologous recombination;

(ii) the resulting differentiated cell or DNA therefrom, wherein the expression of one copy of the IgM gene has been knocked out, is used as a nuclear transfer donor and is fused or inserted into an enucleated oocyte;

(iii) the resulting nuclear transfer unit is allowed to develop into an embryo, and a cell is obtained from this embryo and is contacted with a second DNA construct under conditions that results in the elimination of the expression of the other (second) copy of the IgM gene; by homologous recombination; and

(iv) the resulting cell, in which both copies of the IgM (mu) gene have been knocked out, is used as a nuclear donor for nuclear transfer by fusing or inserting said donor cell or DNA therefrom into an enucleated oocyte or blastomere, activating the resultant nuclear transfer unit after oocyte prior to nuclear transfer, and culturing in a suitable medium to produce a nuclear transfer embryo which does not express IgM heavy chain.

6. (Amended) The method of Claim 1, wherein the differentiated cell of (i) is produced by sequentially contacting said cell with two knockout constructs which in combination provide for knockout of both copies of the IgM genes.

7. (Amended) The method of Claim 6, wherein the said two knockout constructs comprise different selectable markers thereby providing for the selection of cells wherein both copies of the IgM heavy chain are eliminated.

15. (Amended) A transgenic ungulate wherein both copies of the IgM heavy chain (mu) have been knocked out.